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Gestational diabetes mellitus and exposure to ambient air pollution and road traffic noise: A cohort study

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ABSTRACT

Background: Road traffic is a main source of air pollution and noise. Both exposures have been associated with type 2 diabetes, but associations with gestational diabetes mellitus (GDM) have been studied less.
Objectives: We aimed to examine single and joint associations of exposure to air pollution and road traffic noise on GDM in a prospective cohort.
Methods: We identified GDM cases from self-reports and hospital records, using two different criteria, among 72,745 singleton pregnancies (1997–2002) from the Danish National Birth Cohort. We modeled nitrogen dioxide (NO_2) and noise from road traffic (L_{den}) exposure at all pregnancy addresses.
Results: According to the two diagnostic criteria: the Danish clinical guidelines, which was our main outcome, and the WHO standard during recruitment period, a total of 565 and 210 women, respectively, had GDM. For both exposures no risk was evident for the common Danish criterion of GDM. A 10-μg/m^3 increase in NO_2 exposure during first trimester was, however, associated with an increased risk of WHO-GDM (adjusted odds ratio (OR) = 1.24; 95% confidence interval (CI): 1.03, 1.49). The corresponding OR associated with a 10-dB higher road traffic noise level was 1.15 (0.94 to 1.18). In mutually adjusted models the OR for NO_2 remained similar 1.22 (0.98, 1.53) whereas that for road traffic noise decreased to 1.03 (0.80, 1.32). Significant associations were also observed for exposure averaged over the 2nd and 3rd trimesters and the full pregnancy.
Conclusions: No risk was evident for the common Danish criterion of GDM. NO_2 was associated with higher risk for GDM according to the WHO criterion, which might be due to selection bias.

1. Introduction

Worldwide the prevalence of diabetes, including gestational diabetes mellitus (GDM), is rising and type 2 diabetes is a major contributor to the global burden of disease (van Dieren et al., 2010). The increase in prevalence coincides with an increase in urbanization and several changes in lifestyle such as reduced physical activity, increase in calorie-rich diet, obesity and older maternal age at conception. However, better knowledge of modifiable risk factors is urgently needed to target preventive strategies particular among vulnerable populations such as women in the reproductive age.

Pregnancy is a particularly vulnerable period for development of abnormal glycaemia because insulin resistance increases as part of adaption to ensure nutrients transfer to the fetus. GDM is defined as

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glucose intolerance with onset or first recognition in pregnancy affecting up to 14% of pregnancies in the United States (American Diabetes Association, 2004) and 2% in Denmark (Buckley et al., 2012; Ovesen et al., 2015). Women with GDM are more likely to develop preeclampsia and diabetes in the years following pregnancy, and their children are at increased risk of stillbirth, delivery by Cesarean section, macrosomia, overweight, impaired glucose tolerance and diabetes later in life (Clausen et al., 2008; Lawlor et al., 2011; Wendland et al., 2012).

Ambient air pollution and noise from road traffic are widespread exposures that affect large proportions of the population worldwide. Exposure to ambient air pollution has been associated with type 2 diabetes incidence (Andersen et al., 2012; Krämer et al., 2010) and diabetes-related mortality in adults (Raaschou-Nielsen et al., 2013). A recent meta-analysis of European and North American studies on fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) has reported stronger associations between ambient air pollution and type 2 diabetes in women as compared with men (Eze et al., 2015). While several studies have evaluated the associations between air pollution and adverse birth outcomes such as low birth weight (Pedersen et al., 2013; Stieb et al., 2012) and pregnancy-induced hypertensive disorders (Pedersen et al., 2014, 2017), less is known about the associations with GDM.

Exposure to $PM_{2.5}$ as well as higher residential neighborhood traffic density have been associated with impaired glucose tolerance during pregnancy, a milder form of glucose intolerance than GDM in women from the US and Taiwan (Fleisch et al., 2014; Lu et al., 2016). For GDM the current evidence is mixed. There is supporting evidence for an association between exposure to $PM_{2.5}$ and ozone (Hu et al., 2015) as well as nitrogen oxides (NO_X) and GDM from some studies (Malmqvist et al., 2013; Robledo et al., 2015), but others did not find an association (Fleisch et al., 2014, 2016; van den Hooven et al., 2009; Robledo et al., 2015; Yorifuji et al., 2015). Differences in study design such as the criterion used to define GDM may have contributed to the inconsistent results. Moreover, some of the previous studies relied on a very low number of cases ($n < 150$; Fleisch et al., 2014, 2016; van den Hooven et al., 2009; Yorifuji et al., 2015); the larger birth register studies lack information on potential confounders such as pre-pregnancy body-mass index (BMI) (Hu et al., 2015; Robledo et al., 2015), maternal race/ethnicity and education (Malmqvist et al., 2013) and some studies are limited by their crude exposure assessment, which does not take into account fine-scale (Lu et al., 2016; Robledo et al., 2015), temporal variation in air quality (van den Hooven et al., 2009; Yorifuji et al., 2015) or relied on proximity of traffic as a proxy for air pollution exposure (van den Hooven et al., 2009).

The biological mechanisms underlying a possible association between air pollution and GDM are not fully understood. The potential mechanisms of air pollution induced effects observed in experimental studies with rodents (Haberzettl et al., 2016; Xu et al., 2011) and epidemiological studies include impaired endothelial function, elevated oxidative stress and inflammation, all of which have been proposed to be involved in the development of diabetes (Eze et al., 2015).

Since road traffic is a main source of both air pollution and noise mutual confounding is a concern (Tétreault et al., 2013). Exposure to traffic noise may induce a stress response and disturb sleep (Miedema and Vos, 2007). Reduced sleep duration and quality of sleep may elevate the risk for impaired glucose metabolism, insulin resistance, type 2 diabetes and may also contribute to increased risk of gestational diabetes (O'Keeffe and St-Onge, 2013).

The objective of our study was to estimate single and joint associations of exposure to ambient air pollution with road traffic noise and GDM in a large prospective cohort of pregnant women.

2. Methods

2.1. Study population

This study included women who participated in the Danish National Birth Cohort (DNBC, Olsen et al., 2001). Briefly, all general practitioners in Denmark were invited to recruit pregnant women for the cohort. In total, 50% of the general practitioners participated, and 60% of the women invited agreed to participate. Enrollment occurred in gestational weeks 6 to 10 from 1996 to 2002 and computer-assisted telephone interviews with follow-up interviews started around the 12th gestational weeks. Women were only ineligible if they spoke sufficient Danish and intended to carry their pregnancy to term. Written informed consents were obtained from all participants at enrollment. The Danish Data Protection Agency approved the present study (J.nr. 2014-41-3286).

The DNBC includes approximately 35% of all deliveries in Denmark during the recruitment period corresponding to a total number of 101,002 pregnancies. We excluded women from the original cohort due to multiple pregnancies ($n = 2076$), abortions, molar or extra-uterine pregnancies ($n = 5904$), emigration, death or withdrawals of participation in the study (71) and stillborn birth ($n = 303$). For assessment of women at risk and for comparison of results with our previous study on pregnancy-induced hypertension (Pedersen et al., 2017), women who either reported pre-existing hypertension in the pregnancy interview or had a diagnosis of pre-existing chronic hypertension and/or diabetes before pregnancy were excluded ($n = 942$). Information on diagnosis of the relevant diseases used for exclusion of women was retrieved from the Danish National Patient Register (DNPR, Lynge et al., 2011), using the International Classification of Diseases, 10th Revision (ICD-10 codes: O10 for hypertension before pregnancy, I10–I15 for hypertensive diseases, and O24.1–O24.3 for pre-existing diabetes) and self-reported information on pre-existing hypertension from the pregnancy interviews. Furthermore, women with missing information on exposure ($n = 324$), outcomes ($n = 2566$) or covariates ($n = 8494$) were excluded. Finally, we excluded data from later pregnancies for women who had participated in the cohort with more than one pregnancy ($n = 7579$). This rendered a total of 72,745 women in the present study (72% of the source population).

2.2. Gestational diabetes mellitus

The main outcome in this paper is the presence of GDM according to the recommended criterion used for many years in Denmark (Damm et al., 1993; Jensen et al., 2003; Ovesen et al., 2015). During the time period for data collection for the DNBC, GDM screening in Denmark was based on risk factors and fasting blood glucose. Women with risk factors for GDM (family history of diabetes mellitus, 20% overweight or more in the non-pregnant state, previous unexplained stillbirth, previous delivery of a baby with birth weight ≥ 4500 g, age ≥ 35 years, GDM in previous pregnancy, glucosuria) were selected for screening in early pregnancy. If the fasting blood glucose level was 4.1 mmol/L (74 mg/dL) (corresponding to a plasma glucose value of 4.7 mmol/L [85 mg/dL]) or more on two occasions during the routine midwife visits, then a 75 g oral glucose tolerance test (OGTT, 2 h) was performed. If the fasting blood glucose level was lower than 4.1 mmol/L, the procedure with measurements of fasting glucose levels and OGTT was repeated in the third trimester (gestational weeks 30 to 32). Glucose was in most departments measured in capillary blood while venous plasma was used in some departments with standard curves for both. For venous plasma the OGTT was considered abnormal (GDM) if two or more glucose values exceeded 6.2 mmol/L at 0 min, 10.9 mmol/L at 30 min, 11.1 mmol/L at 60 min, 9.2 mmol/L at 90 min, 8.9 mmol/L at 120 min, 8.2 mmol/L at 150 min, and 7.3 mmol/L at 180 min. Glucosuria, detected at any point during pregnancy was followed by screening with fasting glucose/OGTT as described, provided that this